The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 2-7 and 10-23 are rejected under 35 U.S.C. § 103 as being unpatentable over Maekawa et al. in view of Maniatis and further in view of Sudoh et al. (R) and Sudoh et al. (T), and Oikawa et al. and Vlasuk et al., and is repeated for the same reasons of record as found in the Official Action mailed 1/22/93.

Applicant's arguments filed 7/21/93 have been fully considered but they are not deemed to be persuasive.

Applicants cite Sleihammer et al. (U.S. Pat. No. 5,114,923, cited as '923 hereafter) as a teaching away from the expectation

of utilizing the known porcine cDNA (see Maekawa et al.) as a probe to isolate the human BNP DNA.

'923 teaches and claims the human brain natriuretic peptide (hBNP hereafter) amino acid sequence. '923 teaches that a porcine cDNA probe as shown in Figure 1 was unable to isolate the human BNP DNA from a genomic library. However, '923 teaches the isolation of the canine, rat, cat and rabbit DNA encoding BNP from genomic libraries was successful utilizing the porcine BNP cDNA as shown in Figure 1. Figure 2 of '923 shows a portion of the nucleotide sequence of Figure 1 used as a probe. The human BNP DNA was isolated utilizing the canine BNP CDNA shown in Figure 3. It is never disclosed in '923 what explicit porcine BNP probe was utilized in the failed screening of a genomic human library. No analysis or discussion is provided as to why the isolation of canine, rat and rabbit BNP DNAs were successful via a probe based on the porcine cDNA, but failed for the human. Was the same experiment performed for each? No objective analysis of '923's failure can be made, and thus, the merits of this failure can not be judged.

It is alleged by applicants that the failure of '923 to isolate the hBNP DNA using the pBNP cDNA as a probe is an unexpected outcome, and thus teaches away from using the pBNP cDNA as a probe to isolate the human cDNA version. This is not agreed with since no objective experimental methods or results are provided which can be evaluated so as assess the merits of

the experiment. '923 provides only Figure 1 as the probe, which is the entire pBNP cDNA (and a oligonucleotide probe in Figure 2 encoding nucleotides 664-723 of the pBNP cDNA of Figure 1), the hybridization conditions and the simple conclusion at col. 9, lines 45-50:

> "Human genomic DNA did not hybridize to the DNA sequence of Fig. 1 under these conditions [The hybridization conditions set forth in col. 9, lines 38-44.] ..."

It is not clear what was used as a probe. While it is not doubted that '923 used a pBNP probe based on the pBNP cDNA of Figure 1, and further that this probe failed to hybridize to the human DNA version of BNP, the fact that no experimental methods, such as disclosure of the actual probe used, and/or a review of the actual data and results obtain, one is left to simply trust the disclosure of '923 that the proper experiments were performed and show in fact that the pBNP cDNA is not appropriate as a probe for isolation of the human DNA. Note that the Sudoh et al. (Biochem. Biophys. Res. Comm. 159:1427-1434, 1989), while published after applicants filing nonetheless successfully use the porcine cDNA, specifically nucleotides 92-131 as per the Maekawa et al. (Biochem. Biophys. Res. Comm. 157:410-416, 1988) numbering of the pBNP cDNA, as a probe to isolate the hBNP cDNA from a cDNA library with no problems reported. This further casts doubt as to the reliability of applicants conclusion concerning the '923 pBNP probe failure to isolate the human BNP DNA.

Note that '923 screened a genomic library where one would expect less success in seeing a hybridization signal then if one were dealing with a cDNA library which is inherently enriched with the desired DNA. Note also that for a genomic library introns may also cause failure of a cDNA probe since a cDNA lacks the intervening sequences (introns). Additionally, pools of mixed probes are usually tested and not just one probe as is seemingly tested by the specification.

Additionally, two facts from the prior art provide a reasonable expectation that the pBNP cDNA would have successfully been used as a probe to isolate the human BNP (hBNP) from a brain library: 1) Sudoh (R) show in figure 2 that pBNP and hANP are highly homologous and 2) Oikawa et al. and Vlasuk et al. teach that the cDNAs of ANP can be used to isolate the cDNAs of other species (specifically the human ANP cDNA was used to successfully isolated the dog, rabbit and bovine cDNAs). Thus, given from 1) above that BNP and ANP are highly related and homologous natriuretic peptides and from 2) that ANP can be isolated across species in mammalia (an art analogous gene and peptide), one of ordinary skill would have reasonably expected that BNPs would have been found across mammalia, in nervous tissue such as brain just as ANPs are found in atrial or cardiac tissue across mammalia, and that one BNP cDNA would have been reasonably expected to isolate BNP cDNAs across mammalia as is the case for ANPs.

Further, while '923 may provide a teaching away, note that this patent was not available as prior art, and thus the state of the art was silent as to this failure until May of 1992.

THIS ACTION IS HADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Examiner LeGUYADER at telephone number (703) 308-0447.

John L. LeGUYADER
October 1, 1993

RICHARD A. SCHWARTZ
SUPERVISORY PATENT EXAMINER
ART UNIT 185